

What is claimed is:

1. A method to treat a Reelin deficiency or dysfunction, comprising administering to a patient diagnosed with or suspected of having a Reelin deficiency or dysfunction an amount of a polyunsaturated fatty acid (PUFA) selected from the group 5 consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof, to compensate for the effects of Reelin deficiency or dysfunction in the patient.
2. The method of Claim 1, wherein the Reelin deficiency or dysfunction is associated with a decrease in the expression or function of a fatty acid binding protein in the patient.
- 10 3. The method of Claim 2, wherein the fatty acid binding protein is a brain lipid binding protein (BLBP).
4. The method of Claim 1, wherein administration of the PUFA to the patient compensates for reduced fatty acid binding protein or function thereof in the patient.
- 15 5. The method of Claim 1, wherein administration of the PUFA to the patient compensates for reduced brain lipid binding protein or function thereof in the patient.
6. The method of Claim 1, wherein administration of the PUFA to the patient improves the activity of fatty acid binding proteins in the patient.
- 20 7. The method of Claim 1, wherein administration of the PUFA to the patient improves at least one parameter of the mechanism of action of brain lipid binding proteins in the patient.
8. The method of Claim 1, wherein administration of the PUFA to the patient results in increased incorporation of functional DHA into the phospholipid membranes of glial cells and neurons in the patient.
- 25 9. The method of Claim 1, wherein administration of the PUFA to the patient increases the level of Reelin or improves the activity of Reelin in the patient.
10. The method of Claim 1, wherein the patient suffers from a disease or condition associated with the Reelin deficiency or dysfunction, and wherein administration of the PUFA to the patient improves at least one symptom of the disease or condition.
- 30 11. The method of Claim 1, wherein the patient is at risk of developing a disease or condition associated with the Reelin deficiency or dysfunction, and wherein administration of the PUFA to the patient prevents or delays the onset of the disease or condition.

12. The method of Claim 1, wherein, prior to the step of administering, the method comprises measuring an amount or a biological activity of Reelin in a biological sample from the patient.

13. The method of Claim 12, further comprising comparing the amount of 5 Reelin in the patient sample to a baseline amount of Reelin in a sample of the same type, wherein a change in the amount of Reelin in the patient sample as compared to the baseline amount indicates that the patient has a Reelin deficiency.

14. The method of Claim 12, wherein the step of measuring is performed by a method selected from the group consisting of: mRNA transcription analysis, Western 10 blot, immunoblot, enzyme-linked immunosorbant assay (ELISA), radioimmunoassay (RIA), immunoprecipitation, surface plasmon resonance, chemiluminescence, fluorescent polarization, phosphorescence, immunohistochemical analysis, matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, microcytometry, microarray, microscopy, fluorescence activated cell sorting (FACS), flow cytometry, and 15 protein microchip or microarray.

15. The method of Claim 12, further comprising determining the relative expression or activity of different Reelin size forms in the patient to establish a Reelin size form profile in the patient sample, and comparing the patient Reelin size form profile to a baseline profile of Reelin size forms in a sample of the same type, wherein a change 20 in expression of one or more size forms of Reelin as compared to relative expression or activity of the size forms in the baseline profile indicates that the patient has a Reelin deficiency or dysfunction.

16. The method of Claim 15, wherein the step of measuring is performed using a technique selected from the group consisting of: mRNA transcription analysis, 25 Western blot, immunoblot, and capillary electrophoresis.

17. The method of Claim 12, further comprising comparing the activity of Reelin in the patient sample to a baseline activity of Reelin in a sample of the same type, wherein a change in the level of activity of Reelin in the patient sample as compared to the baseline level indicates that the patient has a Reelin dysfunction.

30 18. The method of Claim 17, wherein the step of measuring the activity is by a technique selected from the group consisting of: a receptor-ligand assay and a phosphorylation assay.

19. The method of Claim 12, further comprising measuring the levels of thyroid stimulating hormone (TSH) in the patient sample and comparing the amount of TSH in the patient sample to a baseline amount of TSH in a sample of the same type, wherein a change in the amount of TSH in the patient sample as compared to the baseline amount indicates that the patient has a TSH deficiency.

5 20. The method of Claim 19, further comprising administering a thyroid medication in conjunction with the PUFA, to the patient.

10 21. The method of any one of Claims 12-20, wherein the biological sample is selected from the group consisting of a cell sample, a tissue sample, and a bodily fluid sample.

22. The method of Claim 21, wherein the biological sample is a blood sample.

23. The method of Claim 1, further comprising monitoring the efficacy of the administration of the PUFA on Reelin levels or biological activity in the patient at least one time subsequent to the step of administering.

15 24. The method of Claim 1, further comprising monitoring the efficacy of the administration of the PUFA on changes in the expression or biological activity of one or more size forms of Reelin in the patient at least one time subsequent to the step of administering.

20 25. The method of Claim 23 or Claim 24, further comprising adjusting the administration of the PUFA to the patient in subsequent treatments based on the results of the monitoring of efficacy of the treatment.

26. The method of Claim 1, wherein the patient has, is suspected of having, or is at risk of developing, a neurological disorder or neuropsychiatric disorder.

27. The method of Claim 1, wherein the patient suffers from seizures.

25 28. The method of Claim 1, wherein the patient has, is suspected of having, or is at risk of developing, an autoimmune disorder associated with a neurological dysfunction.

29. The method of Claim 1, wherein the patient has an anti-phospholipid disorder.

30 30. The method of Claim 1, wherein the patient has, is suspected of having, or is at risk of developing, a disorder selected from the group consisting of: schizophrenia, bipolar disorder, dyslexia, dyspraxia, attention deficit hyperactivity disorder (ADHD), epilepsy, autism, Parkinson's Disease, senile dementia, Alzheimer's Disease, peroxisomal

proliferator activation disorder (PPAR), multiple sclerosis, diabetes-induced neuropathy, macular degeneration, retinopathy of prematurity, Huntington's Disease, amyotrophic lateral sclerosis (ALS), retinitis pigmentosa, cerebral palsy, muscular dystrophy, cancer, cystic fibrosis, neural tube defects, depression, Zellweger syndrome, Lissencephaly, 5 Down's Syndrome, Muscle-Eye-Brain Disease, Walker-Warburg Syndrome, Charcot-Marie-Tooth Disease, inclusion body myositis (IBM) and Aniridia.

31. The method of Claim 1, wherein the patient has a thyroid disorder.
32. The method of Claim 1, wherein the PUFA is administered to the patient in combination with one or more additional therapeutic compounds for treating a 10 condition associated with a Reelin deficiency or dysfunction.

33. A method of modulating Reelin expression in tissues or fluids, comprising administering to a patient an amount of a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof, effective to modulate Reelin expression in a tissue or fluid of the patient.

- 15 34. The method of Claim 33, wherein the amount of the PUFA is sufficient to increase Reelin expression in a tissue or fluid of the patient.

35. A method to prevent, reduce or delay the onset of retinal developmental defects or disorders, comprising administering to the patient a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, 20 or a precursor or source thereof, effective to prevent, reduce or delay the onset of retinal developmental defects or disorders and to compensate for the effects of Reelin deficiency or dysfunction in the patient.

36. A method to prevent, reduce or delay the onset of developmental defects or disorders associated with Reelin deficiency or dysfunction, comprising:

- 25 a) measuring the expression or biological activity of Reelin in a biological sample from a patient;
- b) administering to the patient a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof, wherein the amount of the PUFA administered is 30 determined based on the measurement of expression or biological activity of the Reelin in the sample.

37. The method of Claim 36, wherein the step of measuring the expression or activity of Reelin further comprises determining the relative expression or activity of individual size forms of Reelin in the sample.

5 38. The method of Claim 36, wherein the amount of PUFA administered to the patient is determined by comparing the level of expression or biological activity of Reelin in the patient sample to a baseline level of Reelin expression or activity that corresponds to a recommended dosage of the PUFA, and adjusting the dosage of the PUFA for the patient accordingly.

10 39. The method of Claim 38, wherein the amount of PUFA administered to the patient is increased relative to the recommended dosage of PUFA when the expression or biological activity of Reelin in the patient is decreased relative to the baseline level.

15 40. The method of Claim 36, wherein the amount of PUFA administered to the patient is determined by comparing the expression or activity of different Reelin size forms in the patient sample to a baseline profile of Reelin size forms that corresponds to a recommended dosage of PUFA, and adjusting the dosage of the PUFA for the patient accordingly.

20 41. The method of Claim 40, wherein the amount of PUFA administered to the patient is increased relative to the recommended dosage of PUFA when the relative expression or activity of one or more Reelin size forms in the patient sample differs from the relative expression or activity of the Reelin size form in the baseline profile.

42. The method of Claim 36, wherein the step of measuring the expression or biological activity of Reelin in a biological sample from the patient is repeated one or more times subsequent to the administration of the PUFA to the patient.

25 43. The method of Claim 42, wherein the amount of PUFA administered to the patient is adjusted according to the repeated measurement of the expression or biological activity of Reelin in the patient.

30 44. The method of Claim 36, wherein the step of measuring the expression or biological activity of Reelin in a biological sample from the patient is repeated intermittently throughout a portion of the life of the patient or throughout the entire life of the patient, and wherein the amount of PUFA administered to the patient is adjusted to correspond to each new measurement of the expression or biological activity of Reelin in the patient.

45. The method of Claim 36, wherein the expression or biological activity of Reelin in the patient is substantially normal, and wherein the PUFA is administered as a supplement to prevent or reduce the risk of development of Reelin deficiency or dysfunction.

5        46. The method of Claim 36, wherein the patient is a pregnant female.

47. The method of Claim 36, wherein the patient is a lactating female.

48. The method of Claim 36, wherein the patient is a human adult.

49. The method of Claim 36, wherein the patient is a human child or adolescent.

10      50. The method of Claim 36, wherein the patient is a human embryo or fetus and wherein the PUFA is administered to the embryo or fetus by administering the PUFA to the mother of the embryo or fetus.

15      51. The method of Claim 36, wherein the patient has or is at risk of developing a neurological disorder or neuropsychiatric disorder associated with Reelin deficiency or dysfunction or a fatty acid binding protein deficiency.

52. The method of Claim 36, wherein the patient has or is at risk of developing an autoimmune disease associated with Reelin deficiency or dysfunction or a fatty acid binding protein deficiency.

20      53. The method of Claim 36, wherein the patient has or is at risk of developing a developmental defect associated with Reelin deficiency or dysfunction or a fatty acid binding protein deficiency.

25      54. A method to monitor the levels of DHA in the brain of a patient, comprising measuring the levels of Reelin expression or biological activity in a biological sample from the patient and estimating the levels of DHA in the brain of the patient based on the measurement of Reelin.

55. The method of Claim 54, further comprising administering an amount of DHA to the patient corresponding to the measured levels of Reelin expression or biological activity.

30      56. The method of Claim 55, wherein the amount of DHA administered is sufficient to compensate for reduced expression or activity of brain lipid binding proteins in the patient or to improve the activity of brain lipid binding proteins in the patient.

57. The method of Claim 54, further comprising comparing the level of Reelin expression or biological activity in the biological sample from the patient to a baseline

level of Reelin expression or biological activity, wherein the baseline level of Reelin expression or biological activity is correlated with a baseline level of DHA in the brain of a subject, wherein the baseline level is established by a method selected from the group consisting of:

- 5           a) establishing a baseline level of Reelin expression or activity from a previous measurement of Reelin expression or activity in a previous sample from the patient, wherein the previous sample was of a same cell type, tissue type or bodily fluid type; and,
- 10           b) establishing a baseline level of Reelin expression or activity from control samples of a same cell type, tissue type or bodily fluid type as the sample from the patient, the control samples having been obtained from a population of matched individuals.

58. The method of Claim 57, wherein an estimated low level of DHA in the brain of the patient as compared to the baseline level of DHA indicates that the patient 15 should be administered an amount of DHA to compensate for the level of DHA in the brain of the patient.

59. A method to predict the efficacy of incorporation of HUFA into the phospholipid membranes in a patient, comprising:

- 20           a) measuring Reelin expression or biological activity in a biological sample from a patient;
- b) comparing the Reelin expression or biological activity in the biological sample to a baseline level of Reelin; and
- 25           c) predicting the patient efficacy of the incorporation of HUFA into phospholipids membranes, wherein a difference in the level of Reelin expression or biological activity in the biological sample as compared to the baseline level of Reelin expression or biological activity indicates a modification in the predicted ability of the patient to efficaciously incorporate HUFA into phospholipids membranes.

60. The method of Claim 59, further comprising prescribing an amount of 30 HUFA to the patient, wherein the amount is determined based on the predicted ability of the patient to efficaciously incorporate HUFA into phospholipids membranes.

61. A method to diagnose a DHA deficiency in a patient, comprising:

- a) measuring Reelin expression or biological activity in a biological sample from a patient;
- b) comparing the Reelin expression or biological activity in the biological sample to a baseline level of Reelin; and,
- c) making a diagnosis of the patient, wherein detection of a difference in the level of Reelin expression or biological activity in the biological sample as compared to the baseline level of Reelin expression or biological activity, indicates a positive diagnosis of DHA deficiency in the patient.

62. The method of Claim 61, wherein detection of a lower level of Reelin expression or biological activity in the biological sample as compared to the baseline level of Reelin expression or biological activity, indicates a positive diagnosis of DHA deficiency in the patient.

63. The method of Claim 61, wherein the biological sample is selected from the group consisting of a cell sample, a tissue sample, and a bodily fluid sample.

64. The method of Claim 63, wherein the biological sample is a blood sample.

65. The method of Claim 61, wherein the step (a) of measuring comprises measuring Reelin mRNA transcription.

66. The method of Claim 65, wherein the step (a) of measuring is by a method selected from the group consisting of reverse transcriptase-PCR (RT-PCR), *in situ* hybridization, Northern blot, sequence analysis, microarray analysis, and detection of a reporter gene.

67. The method of Claim 61, wherein the step (a) of measuring comprises measuring Reelin protein expression.

68. The method of Claim 67, wherein the step (a) of measuring is by a method selected from the group consisting of immunoblot, enzyme-linked immunosorbant assay (ELISA), radioimmunoassay (RIA), immunoprecipitation, surface plasmon resonance, chemiluminescence, fluorescent polarization, phosphorescence, immunohistochemical analysis, matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, microcytometry, microscopy, fluorescence activated cell sorting, flow cytometry, and protein microchip or microarray.

69. The method of Claim 61, wherein the step (a) of measuring comprises measuring Reelin biological activity.

70. The method of Claim 69, wherein the step (a) of measuring is by a method selected from the group consisting of a receptor-ligand assay and a phosphorylation assay.

71. The method of Claim 61, wherein the baseline level is established by a 5 method selected from the group consisting of:

a) establishing a baseline level of Reelin expression or activity in an autologous control sample from the patient, wherein the autologous sample is of a same cell type, tissue type or bodily fluid type as the sample of step (a);

b) establishing a baseline level of Reelin expression or activity that is 10 an average from at least two previous measurements of Reelin expression or activity in a previous sample from the patient, wherein each of the previous samples were of a same cell type, tissue type or bodily fluid type as the sample of step (a), and wherein the previous measurements resulted in a negative diagnosis; and,

c) establishing a baseline level of Reelin expression or activity from 15 control samples of a same cell type, tissue type or bodily fluid type as the sample of step (a), the control samples having been obtained from a population of matched individuals.

72. A method to supplement PUFA in a female during pregnancy and 20 lactation, comprising:

a) measuring the expression or biological activity of Reelin in a biological sample from one or both parents of a fetus or child;

b) administering a polyunsaturated fatty acid (PUFA) selected from 25 the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof to the mother of the fetus or child, wherein the amount of PUFA administered is determined based on the measurement of expression or biological activity of the Reelin in the sample from the parent, wherein the PUFA supplements the PUFA in the female and her fetus or child.

73. The method of Claim 72, wherein the PUFA is administered in an amount 30 sufficient to compensate for reduced expression or activity of brain lipid binding proteins in the fetus or child or to improve the activity of brain lipid binding proteins in the fetus or child.

74. The method of Claim 72, wherein the PUFA is administered in an amount sufficient to decrease the risk of giving birth to an infant with a Reelin deficiency or dysfunction.

5 75. The method of Claim 72, wherein the PUFA is administered in an amount sufficient to decrease the risk of giving birth to a male infant with a Reelin deficiency or dysfunction.

76. The method of Claim 72, wherein the PUFA is administered in an amount sufficient to prevent, delay the onset of, or reduce the symptoms of autism in the mother, child or fetus.

10 77. The method of Claim 72, wherein the PUFA is administered in an amount sufficient to prevent, delay the onset of, or reduce the symptoms of neuronal migration disorders in the mother, child or fetus.

15 78. The method of Claim 72, wherein the PUFA is administered in an amount sufficient to prevent, delay the onset of, or reduce the symptoms associated with Reelin deficiency or dysfunction in the mother, child or fetus.

79. A method to supplement PUFAs in a female during pregnancy and lactation to decrease the risk of birth of infants having or at risk of developing a Reelin deficiency or dysfunction, comprising:

20 a) identifying the gender of the fetus carried by a pregnant female;  
b) administering a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof to the female during all or a portion of the pregnancy and lactation, to decrease the risk that the fetus will be born with or develop after birth a Reelin deficiency or dysfunction, wherein the administration of the PUFA is increased if the fetus is a male as compared to if the fetus is a female.

25 80. A method to prevent, delay the onset of, or reduce a symptom or disorder associated with Reelin deficiency or dysfunction in a child, comprising:

30 a) measuring the expression or biological activity of Reelin in a biological sample from the child; and  
b) administering to the child a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof, wherein the amount of PUFA administered is

determined based on the measurement of expression or biological activity of the Reelin in the sample.

81. The method of Claim 80, wherein the PUFA is provided in an infant formula supplemented with fatty acids comprising DHA and ARA.

5 82. The method of Claim 80, wherein the PUFA is administered in an amount sufficient to compensate for reduced expression or activity of brain lipid binding proteins in the child or to improve the activity of brain lipid binding proteins in the child.

83. The method of Claim 80, wherein the administration of the PUFA is sufficient to prevent, delay the onset of, or reduce the symptoms of autism.

10 84. The method of Claim 80, wherein the administration of the PUFA is sufficient to prevent, delay the onset of, or reduce the symptoms of neuronal migration disorders.

15 85. A method to prevent, delay the onset of, or reduce a symptom of Alzheimer's disease associated with low molecular weight Reelin phenotypes, comprising:

a) identifying patients with Reelin deficiency or dysfunction, including patients with low molecular weight Reelin phenotypes; and

20 b) administering to the patient of (a) a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof sufficient to compensate for the effects of Reelin deficiency or dysfunction in the patient.

25 86. A method to upregulate fatty acid binding proteins in a patient, comprising administering to a patient a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof effective to upregulate FABP.

87. A method to upregulate Reelin expression or activity in a patient, comprising administering to the patient a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof effective to upregulate Reelin expression or activity.

30 88. A method to improve neuronal migration in a patient, comprising administering to the patient a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof effective to improve neuronal migration in the patient.

89. The method of Claim 88, wherein neuronal migration is measured by measuring levels of Reelin expression or activity in the patient.

90. The method of Claim 88, wherein neural function is measured by imaging techniques, and phenotypic evaluation.

5 91. A method to identify neural progenitor cells, comprising detecting Reelin expression or biological activity in a population of cells, wherein a defined level of Reelin expression or biological activity is associated with neural progenitor cells.

92. The method of Claim 91, further comprising selecting the neural progenitor cells for which Reelin expression or biological activity was detected.

10 93. A method to monitor neural development, comprising:  
a) providing a population of cells comprising neural progenitor cells;  
b) detecting Reelin expression or activity in the population of cells;  
c) exposing the population of cells to conditions under which the neural progenitor cells will develop into differentiated neural cells; and  
15 d) monitoring the expression or activity of Reelin in the cells after step (c), to evaluate the development of the neural progenitor cells into differentiated neural cells.

94. The method of Claim 93, further comprising contacting the population of cells of step (a) with a putative developmental regulatory compound prior to or 20 concurrent with step (b), and determining whether the putative regulatory compound affects the development of the neural progenitor cells into differentiated neural cells by detecting Reelin expression or activity in the population of cells.

95. A method to treat or prevent a disorder associated with a deficiency or dysfunction in fatty acid binding proteins, comprising:

25 a) identifying patients with decreased expression or activity of at least one fatty acid binding protein; and  
b) administering to the patient a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof in an amount that is determined to be sufficient to 30 compensate for the effects of the decreased expression or activity of the fatty acid binding protein.

96. The method of Claim 95, wherein the fatty acid binding protein is a brain lipid binding protein (BLBP).

97. The method of Claim 95, wherein the fatty acid binding protein is a fatty acid binding protein in the heart.

98. A method to treat or prevent a disorder associated with reduced activity or dysfunction of a receptor for a fatty acid binding protein, comprising:

5 a) identifying patients with reduced activity or dysfunction of a receptor for a fatty acid binding protein; and

10 b) administering to the patient a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof in an amount that is determined to be sufficient to compensate for the effects of the reduced activity or dysfunction of a receptor for a fatty acid binding protein.

15 99. A pharmaceutical composition comprising an amount of a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof, with at least one therapeutic compound for treatment or prevention of a disorder associated with Reelin deficiency sufficient to compensate for the reduced expression or activity of fatty acid binding proteins in a patient that has or is at risk of developing a Reelin deficiency.

100. The pharmaceutical composition of Claim 99, wherein the therapeutic compound is a thyroid medication.

20 101. A method to diagnose a DHA deficiency in a patient, comprising:

a) measuring Reelin expression or biological activity in a biological sample from a patient;

b) comparing the Reelin expression or biological activity in the biological sample to a baseline level of Reelin;

25 c) measuring thyroid stimulating hormone (TSH) expression or biological activity in a biological sample from a patient;

d) comparing the TSH expression or biological activity in the biological sample to a baseline level of TSH; and,

30 e) making a diagnosis of the patient, wherein detection of a difference in the level of Reelin expression or biological activity in the biological sample as compared to the baseline level of Reelin expression or biological activity, and wherein detection of a difference in the level of TSH expression or biological activity in the biological sample as compared to the baseline level of TSH

expression or biological activity, indicates a positive diagnosis of DHA deficiency in the patient.

102. The method of Claim 102, wherein the biological sample is selected from the group consisting of a cell sample, a tissue sample, and a bodily fluid sample.

5 103. The method of Claim 102, wherein the patient is pregnant or suspected of being pregnant.

104. A method to supplement PUFAs in a female during pregnancy and lactation, comprising:

10 a) measuring the expression and biological activity of Reelin in a biological sample from the mother of a fetus or child;

b) measuring the expression or biological activity of thyroid stimulating hormone in the biological sample;

15 c) administering a polyunsaturated fatty acid (PUFA) selected from the group consisting of an omega-3 PUFA and an omega-6 PUFA, or a precursor or source thereof to the mother of the fetus or child, wherein the amount of PUFA administered is determined based on the measurement of expression or biological activity of the Reelin in the sample from the parent, wherein the PUFA supplements the PUFA in the female and her fetus or child; and

20 d) administering at least one thyroid medication to the mother of the fetus or child if the measurement of Reelin and thyroid stimulating hormone in the sample from the mother is determined to be low as compared to a baseline level of Reelin and thyroid stimulating hormone.

105. method to diagnose a fetal neurodevelopmental disorder, comprising:

25 a) measuring Reelin expression or biological activity in an amniotic fluid sample from a fetus;

b) comparing the Reelin expression or biological activity in the sample to a baseline level of Reelin; and,

30 c) making a diagnosis of the fetus, wherein detection of a difference in the level of Reelin expression or biological activity in the sample as compared to the baseline level of Reelin expression or biological activity, indicates a positive diagnosis of a neurodevelopmental disorder in the fetus.

106. The method of Claim 105, wherein a fetus having a positive diagnosis in (c) is administered an amount of Reelin or reelin gene *in utero* sufficient to treat the neurodevelopmental disorder.

107. The method of Claim 105, wherein a fetus having a positive diagnosis in 5 (c) is administered an amount of Reelin postnatally sufficient to treat the neurodevelopmental disorder.

108. The method of Claim 107, wherein the Reelin is administered in an infant formula.

109. A nutritional supplement or oral pharmaceutical, comprising an amount of 10 Reelin sufficient to delay or prevent the development of a Reelin-deficiency or dysfunction or a disease or condition related thereto.

110. The nutritional supplement or oral pharmaceutical of Claim 109, wherein the supplement is provided in infant formula.

111. The nutritional supplement or oral pharmaceutical of Claim 109, wherein 15 the supplement is provided to an infant by milk produced by the infant's mother, wherein the mother of the infant is supplemented with Reelin prior to or during lactation.

112. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 87, 88, 95, 98, 99, or 104, wherein the PUFA is a highly unsaturated fatty acid (HUFA).

113. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 20 87, 88, 95, 98, 99, or 104, wherein the PUFA is selected from the group consisting of arachidonic acid (ARA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA).

114. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 25 87, 88, 95, 98, 99, or 104, wherein the PUFA is selected from the group consisting of ARA, EPA, and DHA.

115. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 87, 88, 95, 98, 99, or 104, wherein the PUFA is DHA.

116. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 87, 88, 95, 98, 99, or 104, wherein the source of the PUFA is selected from the group 30 consisting of: fish oil, marine algae, and plant oil.

117. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 87, 88, 95, 98, 99, or 104, wherein the PUFA is DHA and wherein the precursor of DHA is selected from the group consisting of:  $\alpha$ -linolenic acid (LNA), eicosapentaenoic acid

(EPA), docosapentaenoic acid (DPA), and blends of precursors selected from the group consisting of LNA, EPA, and DPA.

118. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 87, 88, 95, 98, 99, or 104, wherein the PUFA is administered in a form selected from the

5 group consisting of: a highly purified algal oil comprising the PUFA in triglyceride form, triglyceride oil comprising the PUFA, phospholipids comprising the PUFA, a combination of protein and phospholipids comprising the PUFA, dried marine microalgae, sphingolipids comprising the PUFA, esters, a free fatty acid, a conjugate of the PUFA with another bioactive molecule, and combinations thereof.

10 119. The method of Claim 118, wherein the bioactive molecule is selected from the group consisting of a protein, an amino acid, a drug, and a carbohydrate.

120. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 87, 88, 95, 98, 99, or 104, wherein the PUFA is administered orally.

121. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 15 87, 88, 95, 98, 99, or 104, wherein the PUFA is administered as a formulation comprising the PUFA or precursor or source thereof selected from the group consisting of: chewable tablets, quick dissolve tablets, effervescent tablets, reconstitutable powders, elixirs, liquids, solutions, suspensions, emulsions, tablets, multi-layer tablets, bi-layer tablets, capsules, soft gelatin capsules, hard gelatin capsules, caplets, lozenges, chewable 20 lozenges, beads, powders, granules, particles, microparticles, dispersible granules, cachets, douches, suppositories, creams, topicals, inhalants, aerosol inhalants, patches, particle inhalants, implants, depot implants, ingestibles, injectables, infusions, health bars, confections, cereals, cereal coatings, foods, nutritive foods, functional foods and combinations thereof.

25 122. The method of Claim 121, wherein the PUFA in the formulation is provided in a form selected from the group consisting of: a highly purified algal oil comprising the PUFA, triglyceride oil comprising the PUFA, phospholipids comprising the PUFA, a combination of protein and phospholipids comprising the PUFA, dried marine microalgae comprising the PUFA, sphingolipids comprising the PUFA, esters of the PUFA, free fatty acid, a conjugate of the PUFA with another bioactive molecule, and combinations thereof.

82

123. The method of any one of Claims 1, 33, 35, 36, 60, 72, 79, 80, 81, 85, 86, 87, 88, 95, 98, 99, or 104, wherein the PUFA is administered in a dosage of from about 0.05 mg of the PUFA per kg body weight of the patient to about 200mg of the PUFA per kg body weight of the patient.